Claim 63 depends from Claim 59 or 60, specifying the first predetermined period of time is less than 1 second. As is shown in Figure 6 of the present specification and the '029 application, a denaturation period of less than one second still results in a maximum yield. Since it is better to obtain results quickly, a denaturation time of less than 1 second is advantageous.

Claim 64 depends from Claim 59 or 60, specifying that the lowering in step b) occurs in about 25 seconds or less. Figure 7 of both the present and the '029 specification shows examples of ramp times (the lowering in step b) of about 25 seconds or less. Ramp times of less than about 25 seconds are also shown in Figures 9A-G of both the present specification and the '029 application.

Claim 65 depends from Claim 59 or 60, specifying an average rate for the lowering of temperature in step b) between at least about 1.5°C/second and up to about 4.1°C/second. In Figure 7 of both the present specification and the '029 application, the temperature drop (92 to 55°C) is shown to occur in 25 seconds. In order to achieve such a drop within 25 seconds, the average rate would have to be at least about 1.5°C/second. Rates greater than 1.5°C/second are disclosed in Figures 9A-G of both the present specification and the '029 application. Furthermore, Figure 7 of both the present specification and the '029 application also disclose the temperature drop (92 to 55°C) occurring in 9 seconds. In order to achieve such a drop within 9 seconds, the average rate would have to be up to about 4.1°C/second.

Claim 67 depends from Claim 59 or 60, specifying the difference between the first and second temperatures as being up to about 42°C. Support is found, for example, at page 24, lines 18-21 of the present specification and at page 17, lines 1-4 of the '029 application where denaturation (first) temperatures are given of 90-92°C and annealing (second) temperatures are given of 50-55°C.

Claim 68 depends from Claim 59 or 60, specifying the second predetermined period as being about 5 seconds or less. Figure 7 of both the present specification and the '029 application disclose that a second predetermined time of about 5 seconds or less results in better specificity of amplification than longer durations. Additionally, Figures 9A-G of both

the present specification and the '029 application disclose various lengths for the second predetermined period, from approximately 5 seconds to less than 1 second.

Claim 69 depends from Claim 59 or 60, specifying the second predetermined period as being less than 1 second. Figure 7 of both the present specification and the '029 application disclose that a second predetermined time (annealing time) of less than 1 second still results in maximal yield. Additionally, Figure 9F of the present specification and the '029 application discloses a second predetermined period of less than 1 second.

Claim 70 has been amended to specify the fact that the sample holder has a thermal mass allowing for the requisite heating and cooling cycle to be completed within 30-60 seconds. Support for this amendment can be found at page 23 lines 15-21 of the present specification and page 16 lines 1-7 of the '029 application.

Claim 73 depends from Claim 70, specifying the first predetermined period of time is less than 1 second. As can be seen in Figure 6 of the present specification and the '029 application, a denaturation period of less than 1 second still provides maximal yield. Since it is better to obtain results quickly, a denaturation step of less than 1 second is advantageous.

Claim 74 depends from Claim 70, specifying that the lowering in step b) occurs in about 25 seconds or less. Figure 7 of both the present and the '029 specification clearly shows examples of ramp times (the lowering in step b) of about 25 seconds or less. Ramp times of less than about 25 seconds are also shown in Figures 9A-G of both the present specification and the '029 application.

Claim 75 depends from Claim 74, specifying lowering in step b) occurs in about 9 seconds. Figure 7 of both the present and the '029 specification clearly shows an example of a ramp time (the lowering in step b) of about 9 seconds.

Claim 76 depends from Claim 70, specifying the lowering in step b) occurs at an average rate of between at least about 1.5°C/second and up to about 4.1°C/second. In Figure 7 of both the present specification and the '029 application, the temperature drop (92 to 55°C) is shown to occur in 25 seconds. In order to achieve such a drop within 25 seconds, the rate would have to average at least about 1.5°C/second. Rates greater than 1.5°C/second are

disclosed in Figures 9A-G of both the present specification and the '029 application. Furthermore, Figure 7 of both the present specification and the '029 application also disclose that the temperature drop (92 to 55°C) is can occur in 9 seconds. In order to achieve such a drop within 9 seconds, the average rate would have to be up to about 4.1°C/second.

Claim 78 depends from Claim 70, specifying the difference between the first and second temperatures as being up to about 42°C. Support is found, for example, at page 24, lines 18-21 of the present specification and at page 17, lines 1-4 of the '029 application where the denaturation (first) temperatures of 90-92°C are disclosed and annealing (second) temperatures of 50-55°C are disclosed.

Claim 79 depends from Claim 70, specifying the second predetermined period as being about 5 seconds or less. Figure 7 of both the present specification and the '029 application disclose that a second predetermined time (annealing time) of about 5 seconds or less results in better specificity of amplification than longer durations. Additionally, Figures 9A-G of both the present specification and the '029 application disclose various lengths for the second predetermined period, from approximately 5 seconds to less than 1 second in Figure 9F.

Claim 80 depends from Claim 79, specifying the second predetermined period as being less than 1 second. Figure 7 of both the present specification and the '029 application disclose that a second predetermined time (annealing time) of less than 1 second still results in maximal yield. Additionally, Figure 9F of the present specification and the '029 application discloses a second predetermined period of less than 1 second.

Claim 81 has been amended to more clearly claim that the method of thermal cycling relates to amplification of a nucleic acid.

Claim 84 depends from Claim 81 or 82, specifying the lowering in step b) occurs at a rate of up to about 4.1°C/second. In Figure 7 of both the present specification and the '029 application, the temperature drop (92 to 55°C) is shown to occur in 9 seconds. In order to achieve such a drop within 9 seconds, the rate would have to be at least about 4.1°C/second. Rates less than 4.1°C/second are disclosed in Figures 9A-G of both the present specification

and the '029 application.

Claim 85 depends from Claim 81 or 82, specifying the difference between the first and second temperatures as being up to about 42°C. Support is found, for example, at page 24, lines 18-21 of the present specification and at page 17, lines 1-4 of the '029 application where the denaturation (first) temperatures of 90-92°C are disclosed and annealing (second) temperatures of 50-55°C are disclosed.

Claim 86 depends from Claim 81 or 82, specifying the first predetermined period of time is 8 seconds or less. As is shown in Figure 6 of the present specification and the '029 application, a denaturation period of 8 seconds or less results in optimal product yield.

Claim 87 depends from Claim 81 or 82, specifying that the first predetermined period of time is less than 1 second. As is shown in Figure 6 of the present specification and the '029 application, a denaturation period of less than one second still provides maximal product yield.

Claim 88 depends from Claim 81 or 82, specifying the second predetermined period is about 20 seconds or less. As is shown in Figure 7 of the present specification and the '029 application, a second predetermined period of about 20 seconds or less results in the occurrence of less background amplification and/or degradation of desired product.

Claim 89 depends from Claim 81 or 82, specifying the second predetermined period is less than 1 second. Figure 7 of both the present specification and the '029 application disclose that a second predetermined time (annealing time) of less than 1 second still results in maximal yield. Additionally, Figure 9F of the present specification and the '029 application discloses a second predetermined period of less than 1 second.

Claim 90 depends from Claim 70, specifying a further step of detecting the amplification products. Support for this additional step is found in Figures 6 and 7 of both the present specification and the '029 application, as both figures depict the detection of amplification products.

Applicants submit that the present amendments introduce no new matter.

On the basis of the amendments and remarks presented herein, Applicants believe that this application is now in condition for immediate allowance. Applicants respectfully request that the Examiner pass this application to issue, and early notice of such is requested.

Respectfully submitted,

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VERSIONS SHOWING CHANGES MADE

IN THE CLAIMS:

59. (Amended) A method of subjecting a sample to rapid thermal cycling, said method comprising:

a) contacting a sample holder containing a sample with heated fluid, thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time;

b) contacting the sample holder with non-heated fluid, thereby lowering the temperature of the sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time;

c) contacting the sample holder with heated fluid, thereby raising the temperature of the sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time;

wherein steps a) through c) are completed in about 30-60 seconds; and

wherein said sample holder has a thermal mass which provides for completing said cycle in 30-60 seconds.

65. (Amended) The method of Claim 59 or 60, wherein said lowering in step b) occurs at an average rate of between at least about 1.5 °C per second and up to about 4.1 °C per second.

70. (Amended) A method of amplifying a nucleic acid, said method comprising:

a) heating [contacting] a sample holder containing a sample comprising a nucleic acid and amplification primer [with heated fluid], thereby raising the temperature of the sample to a first temperature, and holding the sample at about said first temperature for a first predetermined period of time to denature said double-stranded nucleic acid;

b) cooling [contacting] the sample holder [with non-heated fluid], thereby lowering the temperature of the nucleic acid sample to a second temperature, and holding the sample at about said second temperature for a second predetermined period of time to anneal said amplification primer;

c) heating [contacting] the sample holder [with heated fluid], thereby raising the temperature of the nucleic acid sample to a third temperature, and holding the sample at about said third temperature for a third predetermined period of time to allow amplification of said nucleic acid; and

d) repeating steps a) through c), wherein steps a) through c) are completed in about 30-60 seconds;

wherein said sample holder has a thermal mass which provides for completing said cycle in 30-60 seconds.

76. (Amended) The method of Claim 70, wherein said lowering in step b) occurs at an average rate of between at least about 1.5 °C per second and up to about 4.1 °C per second.

81. (Amended) A method of subjecting a sample to rapid thermal cycling to amplify a nucleic acid, said method comprising:

a) raising the temperature of a sample to a first temperature and holding the sample at about said first temperature for a first predetermined period of time;

b) lowering the temperature of the sample to a second temperature at a rate at least about 1.5 °C per second and holding the sample at about said second temperature for a second predetermined period of time.

86. (Amended) The method of Claim 81 or 82, wherein the first predetermined period of time is about [64] 8 seconds or less.

88. (Amended) The method of Claim 81 or 82, wherein the second predetermined period of time is about [80] 20 seconds or less.

90. (New) The method of Claim 70, further comprising the step;
e) detecting the amplification products.